The Saudi Dental Journal (2013) **25**, 91–94

King Saud University

The Saudi Dental Journal

www.ksu.edu.sa
www.sciencedirect.com

CASE REPORT

Oral manifestations of lipoid proteinosis: A case report and literature review

S.M. Ravi Prakash *, Sankalp Verma, M.N. Sumalatha, Sayan Chattopadhyay

Oral Medicine and Radiology, Kothiwal Dental College and Research Centre, Mora Mustaqueem, Kanth Road, Moradabad, UP 244001, India

Received 22 May 2012; revised 28 November 2012; accepted 22 December 2012
Available online 20 February 2013

KEYWORDS

Acneiform scars;
Consanguinity;
Hoarseness;
Lipoid proteinosis;
Monoliform blepharosis

Abstract Lipoid proteinosis is an uncommon autosomal recessive metabolic disorder that presents in early life with hoarseness and pox-like acneiform scars involving the skin and mucous membranes. Previous studies have attributed the prevalence of lipoid proteinosis to consanguineous parents. This paper reports a classical case of lipoid proteinosis with oral manifestations but without a history of consanguinity.

1. Introduction

Lipoid proteinosis (LP) was first reported by Seibman in 1908 (Kaur and Singh, 1992). The disorder was initially observed in South Africa, where the responsible gene was introduced in the mid-17th century by a German settler and his sister (Emsley and Paster, 1985; Heyl, 1970). In 1929, Urbach and Wiethe, a dermatologist and otorhinolaryngologist, respectively, from Vienna, described an entity that they called ''lipoidosis cutis et mucosae'' on the basis of histological findings of the deposition of a lipid material associated with protein in the skin and mucous membrane (Urbach and Weithe, 1929). This name was subsequently modified to ''lipoid proteinosis'' to avoid confusion with other lipoidoses (Banerjee et al., 2005). Since its initial report in the literature, over 300 cases of LP have been reported (Parimalam et al., 2009).

As a rare autosomal recessive hereditary disorder characterized by hoarseness of the voice together with skin and mucosal changes, LP (MIM 247100) is caused by homozygous or compound heterozygous mutations in the ECM1 gene located on chromosome 1q21 (Urbach and Weithe, 1929; Salih, 2011). The ECM1 gene encodes an important structural component of the basement membrane and extracellular matrix (Salih, 2011; Hamada et al., 2003; Sercu et al., 2008). The dermatologic manifestations of LP, such as warty skin, scarring, and mucosal thickening, arise from the loss of protein–protein interactions due to ECM1 gene mutations (Salih, 2011; Staut and Naidich, 1998). Similar changes are observed in the nasopharynx, tongue, and vocal cords, resulting in characteristic severe fibrosis and hoarseness. A few cases of LP associated with mild mental retardation have been reported. Other rarely associated neurologic abnormalities include complex partial seizures, amnesia, and mood disturbances, which often begin in the second decade of life (Salih, 2011; Newton et al., 1971).

* Corresponding author. Address: Department of Oral Medicine and Radiology, Kothiwal Dental College and Research Centre, Dhanwantri Nursing Home, Sarai Khalsa, Moradabad, UP 244001, India. Tel.: +91 997119919.
E-mail address: sasan_ravi@rediffmail.com (S.M. Ravi Prakash).

Peer review under responsibility of King Saud University.

ELSEVIER Production and hosting by Elsevier

1013-9052 © 2013 Production and hosting by Elsevier B.V. on behalf of King Saud University.
http://dx.doi.org/10.1016/j.sdentj.2012.12.004

Previous studies have attributed the prevalence of LP to consanguineous parents. Herein, we report a case of LP with oral manifestations but without a history of consanguinity.

2. Case report

A 32-year-old male patient reported to the dental outpatient department complaining of eruptions in the mouth for the previous 25–30 years. Family history was noncontributory, with the absence of consanguinity. The face revealed multiple acneiform scars (Fig. 1); beaded papules on the eyelids; as well as papulovesicular lesions, scars, and hyperkeratosis on the upper and lower extremities, face, and pinnae. Alopecia was also observed. Extra oral examination revealed lacerations on the upper and lower lip secondary to injury (Fig. 2). Intraoral examination revealed a thickened, pale, firm, and enlarged crenated tongue, with yellowish white papule on its surface and a cobblestone appearance. The tongue movements were restricted (Fig. 2). Other findings included hyperkeratosis on the labial, buccal, and palatal mucosa, which gave a thickened and nodular appearance (Fig. 3 and 4). Throat examination by indirect laryngoscopy revealed headed deposits over the epiglottis and vocal cords.

The patient gave his informed consent for the publishing of photographs. Approval for this study was obtained from the local institutional ethics board. The approved protocol included several investigations, such as a routine hemogram and renal and liver function tests. The results of these tests and the radiographic examination of the skull were unremarkable.

Based on the clinical history of the case, a provisional diagnosis of LP was made while the diagnoses of myxoedema, erythropoietic protoporphria, and xanthomas were ruled out. The patient was subjected to an oral mucosal biopsy, which revealed the presence of hypertrophied squamous epithelium showing acanthosis, hyperkeratosis, parakeratosis, and koilocytosis. The underlying fibrous tissue displayed focal areas of hyaline eosinophilic material deposits. These findings confirmed the diagnosis of LP (Fig. 5). A proper oral hygiene regimen was initiated, and the carious breakdown of the teeth was treated. The patient was referred to a dermatologist for the skin changes, followed by proper evaluation and treatment by an otorhinologist for the hoarseness of voice.

Figure 2 Photograph showing lacerations on the upper and lower lip with cobblestone appearance at the dorsum and restricted protrusion of the tongue.

3. Discussion

As a rare autosomal recessive hereditary disorder that is most common among individuals of European descent, LP (Urbach–Wiethe disease) is characterized by the widespread deposit of storage material, particularly in the skin and mucous membranes of the mouth, pharynx, and larynx. This disorder presents in early infancy with hoarseness, pox-like and acneiform scars, and the infiltration and thickening of the skin and certain mucous membranes (Hamada et al., 2003; Hamada, 2005). Similar clinical features were seen in our patient. Although not present in our case, bilateral oval calcification

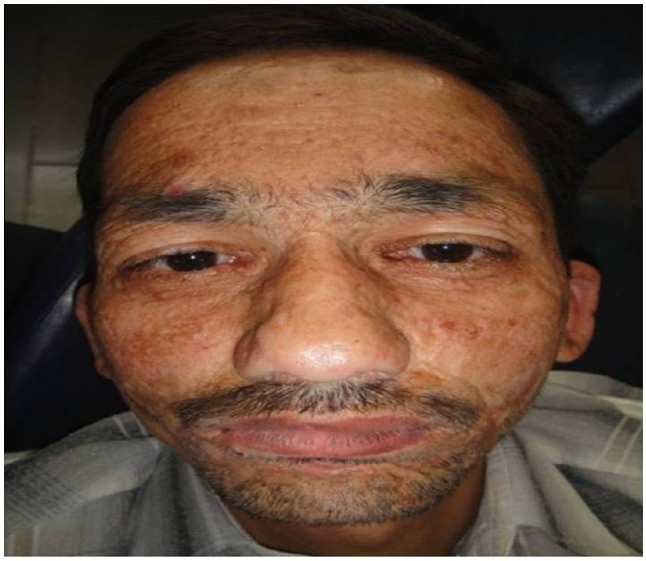

Figure 1 Photograph of the patient showing acneiform scars on the face with beaded papules on the margins of the eyelids.

Figure 3 Photograph showing hyperkeratosis on the left buccal mucosa, giving a thickened and nodular appearance.

Figure 4 Photograph showing hyperkeratosis on the right buccal mucosa, giving a thickened and nodular appearance.

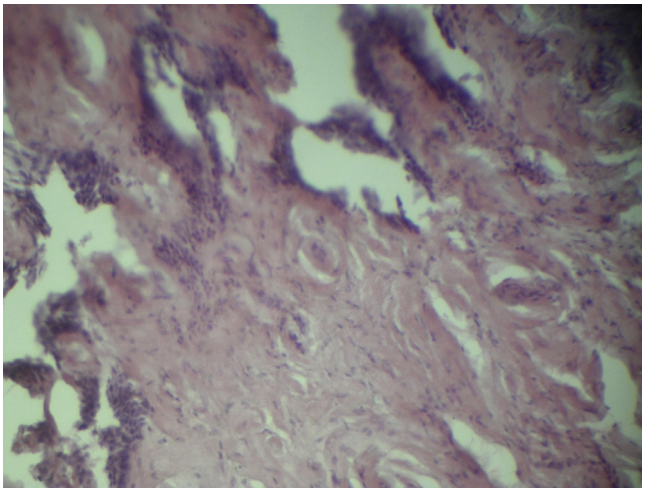

Figure 5 Photograph of the hematoxylin and eosin stained specimen showing acanthosis, hyperkeratosis, parakeratosis and koilocytosis with focal areas of hyaline eosinophillic material deposits (10× magnifications).

in the region of the medial temporal lobes is unique to LP, with a reported incidence of 52% of cases (Javeria et al., 2008).

LP results from mutations in ECM1, a glycoprotein expressed in several tissues, including those of the skin. This glycoprotein is composed of two alternatively spliced isoforms, ECM1a and ECM1b, the latter lacking exon 7 of the 10-exon gene. The mutations map onto chromosome 1q21. Exons 6 and 7 are the most common sites for ECM1 mutations in LP. Clinically, mutations outside exon 7 are usually associated with a slightly more severe mucocutaneous LP phenotype. Neurological features do not show any specific genotype–phenotype correlation (Poyrazoglu et al., 2008).

Symptoms of LP in the newborn include a hoarse cry and skin manifestations, which occur in sequential but overlapping stages and include vesicles, pustules, bullae, and hemorrhagic crusted eruptions on the face and limbs that are more extensive in areas of trauma. Skin manifestations heal with pox-like acneiform atrophic scarring and extracutaneous expressions from the incursion of hyaline-like material in the skin, larynx, and various organs (Javeria et al., 2008). Consequently, cutaneous manifestations become apparent, and the skin eventually becomes thick, yellowish, and waxy. Later, papules, verrucous plaques, and nodules arise on the face, axillae, and scrotum (Parimalam et al., 2009). A pathognomonic sign is a row of beaded papules along the eyelid margins, resembling a string of pearls, termed ''moniliform blepharosis''. The scalp may show alopecia areata. All of these features were observed in our case.

Systemic manifestations of LP include learning and behavioral changes, seizures, dysphagia, and dyspnea. Generalized dystonia and gastrointestinal bleeding are rarely reported. Our patient was of short stature. Several authors have reported that the short stature in LP could be due to defective osteoblasts that are biologically similar to fibroblasts (Chakrabarti et al. 1991; Poyrazoglu et al., 2008). Oral manifestations of LP include papules on the tongue, frenulum, and lips. These papules can cause pebbling of the oral mucosa and a woody tongue that is unable to protrude fully, leading to impaired speech and gustation, transient swelling, and ulceration of the lips and tongue. Similar features were also observed in our case. Other manifestations may include hyperplasia or aplasia of the teeth, as well as recurrent inflammation of the parotid and submandibular glands. Although absent in our case, a pathognomonic finding of LP is bilateral, intracranial, bean-shaped calcifications within the hippocampal region of the temporal lobes of the brain (Parimalam et al., 2009).

LP must be differentiated from erythropoietic protoporphyria (EPP), a condition characterized by skin involvement confined to sun-exposed areas and associated with photosensitivity (Rao et al., 2009). EPP includes the deposition of PAS-positive material that is less dense around the blood vessels and never occurs around the sweat gland coils. LP should also be histologically differentiated from amyloidosis and xanthomas, which are also associated with the deposition of material in the eyelids. In adults, the differential diagnosis includes lichen myxoedema and myxoedema. Our patient underwent oral mucosal biopsy, which revealed the presence of hyaline deposits in the underlying connective tissue, confirming the diagnosis of LP. This disorder is associated with basement membrane thickening at the epithelial connective tissue junction, papillary dermis, surrounding blood vessels, and around the adnexal epithelia, especially the sweat gland coils (Javeria et al., 2008). The only abnormal laboratory finding in LP is an elevated erythrocyte sedimentation rate, which is believed to be caused by the increased production of alpha- and beta-globulins (Hamada, 2005).

LP has a fluctuating course. Despite many therapeutic trials for LP, treatment of this condition remains unsatisfactory. Because consanguinity is prevalent in cases of LP, genetic counseling of the parents should be performed. There is no cure for LP, and the treatment aims at reducing morbidity and preventing complications. Treatment should include patient education, and parents should be told about the risk of having affected offspring. Medical treatment includes oral steroids, dimethyl sulphoxide, intralesional heparin, and etretinate. Surgical care involves resection of the vocal cord papules to improve vocal quality (Javeria et al., 2008). The administration of potent topical steroids and dermabrasion of the skin may help in cosmetic improvement. CO_2 laser can be used to treat lesions of the vocal cord and beaded eyelid papules. Systemic manifestations should be treated appropriately. In particular,

laryngeal obstruction can lead to death if not detected early (Parimalam et al., 2009). According to Azimi and Khodaeiani (2006), treatment with neotigason at 50 mg/day was effective in reducing skin ulceration and dysphagia.

The prognosis of LP is generally good, although the disease is progressive until early adult life. A dental surgeon is often in the earliest position to diagnose LP and refer the patient to a specialist, thereby reducing his or her morbidity.

4. Conflict of interest

None declared.

References

Azimi, H., Khodaeiani, E., 2006. Lipoid proteinosis: successful treatment with neotigason. Med. J. Tabriz Univ. Med. Sci. 28 (4), 129–132.

Banerjee, S. et al., 2005. Lipoid proteinosis with vesicular eruptions and hypertrichosis: rare associations. Indian J. Dermatol. 50 (2), 98–100.

Chakrabarti, K. et al., 1991. Lipoid proteinosis (Urbach–Wiethe syndrome) with dwarfism. Indian pediatr. 28, 75–78.

Emsley, R.A., Paster, L., 1985. Lipoid proteinosis presenting with neuropsychiatric manifestations. J.Neurol. Neurosurg. Psychiatry 48, 1290–1292.

Hamada, T., 2005. Lipoid proteinosis. Orphanet Encyclopedia (February).

Hamada, T. et al., 2003. Extracellular matrix protein 1 gene (Ecm1) mutations in lipoid proteinosis and genotype-phenotype correlation. J. Invest. Dermatol. 120 (3), 345–350.

Heyl, T., 1970. Genealogical study of lipoid proteinosis in South Africa. Br. J. Dermatol. 83, 338–340.

Javeria et al., 2008. Urbach–Wiethe disease: experience at a tertiary care hospital in Abbottabad, Pakistan. J. Ayub. Med. Coll. Abbottabad 20 (4).

Kaur, V., Singh, G., 1992. Lipoid proteinosis. Indian J. Dermatol. Venereol. Leprol. 58, 399–400.

Newton, F. et al., 1971. Neurologic involvement in Urbach–Wiethe's disease (lipoid proteinosis). A clinical, ultrastructural and chemical study. Neurology 21 (12), 1205–1213.

Parimalam, K. et al., 2009. Lipoid proteinosis in a child with recurrent respiratory infection. E-J. Indian Soc. Teledermatol. 3, 4.

Poyrazoglu, S. et al., 2008. Severe short stature: an unusual finding in lipoid proteinosis. J. Clin. Res. Ped. Endo. 1 (2), 97–101.

Rao, R. et al., 2009. J. Oral Maxillofac. Pathol. 13 (2), 81.

Salih, A., 2011. Molecular and neurological characterizations of three Saudi families with lipoid proteinosis. BMC Med. Genet. 12, 31.

Sercu, S. et al., 2008. Interaction of extracellular matrix protein 1 with extracellular matrix components: ecm1 is a basement membrane protein of the skin. J. Invest. Dermatol. 128 (6), 1397–1408 (Errata. 129, 1836–1837).

Staut, C., Naidich, T., 1998. Urbach–Wiethe disease (lipoid proteinosis). Pediatr. Neurosurg. 28 (4), 212–214.

Urbach, E., Weithe, C., 1929. Lipoidosis cutis et mucosae. Virchows Arch. Anat. 273, 285–319.